An 8-year follow-up for a woman with a spinal meningeal melanocytoma in S1 Nerve Root: a case report and literature review

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Case report

Keywords: spinal meningeal melanocytoma, nerve root, HMB-45, surgical resection, literature review

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Abstract

Background: Primary melanocytic neoplasms in the central nervous system (CNS) are rare lesions arising from leptomeningeal melanocytes. These lesions produce neural deficits that resemble those of a meningioma or a schwannoma radiologically Case presentation: A tumor around the left S1 root with an extension into the left paraspinal compartment was identified in a 32-year-old female with persistent left leg pain for 6 months. The tumor was hyper-intense on T1-weighted image and hypo-intense on T2-weighted image with a homogeneous enhancement. The clinical features, radiologic presentations, treatment choice and pathologic characteristic were illustrated. The treatment outcome was compared with those reported in the previous literature. The tumor was en-bloc resected with the S1 nerve root reserved. Grossly, the tumor was a soft, capsulated, well-circumscribed black pigmented lesion. Immunohistochemistry revealed that the tumor cells were positive for HMB-45, S-100 protein and vimentin. The patient's symptoms were greatly relieved postoperatively. No signs of local recurrence were observed. Conclusion Spinal meningeal melanocytoma inside the nerve root is rare and benign. It is difficult to diagnose and often misdiagnosed as schwannoma or meningioma. HMB-45 has been suggested as a significant marker for the diagnosis of meningeal melanocytoma. Complete surgical resection is recommended as the primary treatment. Radiotherapy, chemotherapy and other treatments can be selected as adjuvant therapies, but their effects are controversial. The recurrence and metastasis rates also remain unclear. Key word: spinal meningeal melanocytoma; nerve root; HMB-45; surgical resection; literature review

Background

Primary melanocytic neoplasms in the central nervous system (CNS) are rare lesions arising from leptomeningeal melanocytes. Most localized and pathologically melanotic tumours include melanotic meningioma, melanotic schwannoma, pigmented meningioma, or meningeal melanocytoma..[1,2] Meningeal melanocytoma is rare, benign and solitary tumor located in the intracranial and spinal compartments.[3,4] The variants of meningeal melanocytoma, either extradural or intradural, are often found in the cervical and thoracic spine. These lesions produce neural deficits that resemble those of a meningioma or a schwannoma radiologically.[5]

Here we report a spinal meningeal melanocytoma at the S1 nerve root, illustrate its clinical features, radiologic presentations, treatment choice and pathologic characteristics and compare its treatment outcome with those in the previous literature.

1. Case Presentation

1.1 History, Physical and Laboratory Examinations

The research was approved by ethics committee of Shanghai Longhua Hospital. Written informed consent was obtained from patients for publication of the cases report and any accompanying images. A 32-year-old female visited our hospital, with persistent pain in the left leg for 6 months and no history of

cancer or tuberculosis, recent weight loss, low-grade fever, decreased appetite, or night sweats. She complained of radicular pain which led to numbness and weakness in her left leg, and consequently limited her mobility. The pain was not effectively relieved after using non-steroidal anti-inflammatory drugs (NSAIDs).

At admission, physical examination showed decreased sensation and tenderness in the posterolateral side of her left leg. The Lasegue test was 30° positive in the left leg. Manual muscle testing revealed the strength of the left leg gastrocnemius muscle was in Grade 4 (VAS score 8).

Laboratory studies revealed normal white blood cell count, neutrophil count, hemoglobin level, C-reactive protein (CRP) level and erythrocyte sedimentation rate (ESR). Tumor markers were normal. The purified protein derivative and M-protein electrophoresis tests were negative.

1.2 Imaging Findings

Preoperative plain radiographs, enhanced and reconstructed CT and MRI scans were obtained. The lumbar plain radiograph revealed a straight physiological radian, tilting to the left side. The tumor displayed iso-density on CT scans with no obvious osteolytic lesions. MRI included axial, coronal, and sagittal T1-weighted, T2-weighted and enhanced sequences. MRI image of the lumbar region demonstrated a tumor around the left S1 root with an extension into the left paraspinal compartment. The lesion was hyper-intense on T1-weighted image, hypo-intense on T2-weighted image, and a homogeneous enhancement on contrast-enhanced MRI. However, these imaging findings could not indicate obvious destruction in the vertebral bodies. The radiological appearance suggested a schwannoma.

1.3 Surgical Treatments and Pathologic Findings

L5 laminectomy was performed with the patient in a prone position. The lumbar spine was stabilized with the posterior screw and rod system. At operation, a firm, dark brownish well-encapsulated lesion was found to have reached the nerve sheath of the left S1 spinal nerve root. The dura was compressed and displaced to the right side, and the tumor extended into the left iliopsoas muscle through the enlarged intervertebral foramen. Linear incision over the nerve sheath allowed a sudden gush of darkish hematoma. An en-bloc resection of the tumor was performed using microscopic tumor hook and tumor forceps. The tumor was a soft, capsulated, well-circumscribed black pigmented lesion. The nerve rootlet was decompressed and the S1 nerve root was reserved. A total decompression was achieved without affecting the facet joint.

The pathologic specimens were reviewed after routine hematoxylin-eosin staining for immunological markers. Pathologic examination confirmed the tumor as a melanocytoma. During histopathologic

examination, the morphology of the tumor cells was obscured by extensive pigmentation. After bleaching and eosin staining, light microscopic examination demonstrated an encapsulated cellular tumor composed of sheets of cells with abundant eosinophilic cytoplasm and large vesicular nuclei, rather than a prominent nucleolus. Abundant coarse brown pigment granules were seen in the cytoplasm of many tumor cells. Immunohistochemistry revealed that the tumor cells were positive for homatropine methylbromide (HMB-45), S-100 protein and vimentin, and negative for epithelial membrane antigen and glial fibrillary acidic protein. The Ki-67 labeling index was approximately 5%.

1.4 Follow-up

The patient underwent neither radiotherapy nor chemotherapy and her symptoms were greatly relieved postoperatively. At the latest follow-up, no signs of local recurrence were observed. No spinal instability was found in the postoperative radiographs.

2 Discussion And Conclusion

Meningeal melanocytoma is a rare clinical entity. The term was first introduced by *Limas* and *Tio* in 1972 to describe a group of benign lesions other than pigmented meningiomas, meningothelial fibroblasts and schwannomas. These benign tumors arise from leptomeningeal melanocytes, and resemble the other melanocytic neoplasms of the central nervous system.[6]

The etiology and pathogenesis of spinal meningeal melanocytoma remain unclear. Intradural spinal melanocytoma involving S1 nerve root is an extremely rare case. To the best of our knowledge, 13 spinal meningeal melanocytoma cases have been reported.[6-18] (Table 1) Among them, three were the meningeal melanocytoma in the dorsal region. The follow-up duration of the present case is by far the longest.

The imaging features of meningeal melanocytoma are still illusive. The degree, distribution of melanin pigment and the presence of hemorrhage of the tumor are often considered in diagnosis. In CT scan, meningeal melanocytoma is manifested as iso- to high-density lesions that can be enhanced by contrast media. In MRI, due to the paramagnetic effect of melanin (PEDDPRE effect), the tumor shows hyper- or iso- intense in T1-weighted images and iso- or slightly hypo- intense in T2-weighted images.[15,19,20] But, these radiological manifestations are debatable, usually leading to misdiagnosis of a schwannoma or meningioma. Spinal schwannoma tends to have a signal intensity equal to or less than that of the spinal cord on T1-weighted images. Meningioma usually shows iso- or hyper-intense signals on T2-weighted images, and diffuse enhancement on contrast-enhanced T1-weighted images.[21,22] Furthermore, MRI images were sorted into four groups based on putative patterns by *Isiklar*: (1) melanotic type: hyper-intense in cortex on T1-weighted images, hypo-intense in cortex on T2-weighted images, and iso- or hyper-intense in cortex on proton density-weighted images; (2) amelanotic type: hypo-intense or iso-intense in

cortex on T1-weighted images and hyper-intense or iso-intense in cortex on T2-weighted and proton density weighted images; (3) indeterminate, or mixed type: MR imaging characteristics not conforming to those of one of the first two categories; and (4) hematoma type: MR imaging features exhibiting only hematoma.[23]the meningeal melanocytoma in this case is of melanotic type: hyper-intense in cortex on T1-weighted images, hypo-intense in cortex on T2-weighted images, and iso- or hyper-intense in cortex on proton density-weighted images.

The treatment for spinal meningeal melanocytoma has not been standardized. Complete surgical resection has the best efficacy.[12,20,24,25] However, the resectability is sometimes weakened by the involvement of vital structures (such as nerve root). There is little evidence regarding the efficacy of radiotherapy for meningeal melanocytoma. In cases of incomplete resection, adjuvant postoperative radiotherapy is advised. Some scholars hold that the benign melanocytoma with an aggressive course should receive complete surgical resection. Therefore, adjuvant radiotherapy (30–54 Gray) is recommendable for both complete and incomplete resection.[26,27] In addition, radiosurgery has been used in special cases.[28] Some patients are advised to receive postoperative chemotherapy (DAV) as follows: dacarbazine, 150 mg/day intravenously for 5 days; vincristine, 1 mg/day for 1 day; and ACNU, 100 mg/day for 1 day. This therapy is repeated for three cycles at 1-month intervals. But the benefit of chemotherapy is limited[29] and unrecommendable.

Some literatures have discussed the impact of therapeutic options. *Rades* reviewed 89 intracerebral and spinal melanocytomas recurring within 5 years after surgery. The survival rates were reported as follows: complete resection, 100%; complete resection plus radiotherapy, 100%; incomplete resection plus radiotherapy, 100%; and incomplete resection alone, 46%.[30] *Roser* found that the recurrence rate within two years after complete resection and incomplete resection with radiotherapy was significantly higher than that after incomplete resection alone. So, complete resection was also the best therapeutic option.[31]

The diagnosis of meningeal melancytoma was confirmed by histopathologic and immunohistochemical tests. Characteristic immunohistochemical properties of meningeal melanocytoma include positive responses to HMB-45, S-100 protein and vimentin. Positive response to HMB-45 favors the tumor of melanocytic origin. S-100 protein can be found not only in cells prone to melanogenesis, but also cells from neuroectoderm. About 10% of malignant melanoma cells are negative for S-100 protein. Therefore, the negativity to S-100 protein cannot exclude the odds of malignant melanoma, and other indicators are needed for diagnosis.[15,31] The negativity for epithelial membrane antigen (EMA) can rule out the possibility of meningioma, and the negativity for Leu 7 can rule out schwannoma.[10,32] Ki-67 labeling index (>3%) can also assist the diagnosis of meningeal melancytoma. In the present case, immunohistochemical tests revealed that the tumor cells were positive for HMB-45, S-100 protein and Vimentin, and negative for EMA. The Ki-67 labeling index was approximately 5%.[33-36]

The World Health Organization has classified meningeal melanocytoma into three categories: low grade (melanocytoma), high grade (melanoma), and intermediate-grade.[4,37] The present case was diagnosed

as low grade melanocytoma. The absence of cellular pleomorphism and rare mitoses often eliminate its malignancy. So the lesion usually has a benign course and a good prognosis. Microscopically, meningeal melanocytoma, usually appears dark-brown or black, nodular and encapsulated, and demonstrates spindle or epithelioid cells with relatively well-defined eosinophilic cytoplasm, centrally-located vesicular nuclei and brown-pigmented granules.[1,38-40] Ultrastructurally, the meningeal melanocytoma cells are characterized by of polar cytoplasmic processes, scarce zonula adherens and numerous premelanosomes at different stages of differentiation.[41,42] Benign melanocytoma may show an aggressive course to malignancy, and even recur after complete excision.[30,43-45] Malignancy has been rarely reported in the literature. Most reported malignant cases develop solitary lesions with slow growth and low infiltration.[36,46] *Litofsky* summarized the characteristics of benign lesions: (1) a history of more than one year; (2) similar imaging characteristics to meningioma; (3) dominant spindle cells with lower mitotic rate.[25] *Rades* reviewed all the reported cases and found that the 5-year local control rate was 78% after complete resection.[27] *Oruckaptan* said that spinal localizations had lower recurrence rates (13%) than cranial lesions (29%).[41] In the present case, we performed a gross total resection and the symptoms relieved dramatically after the operation. No signs of local recurrence was seen during the 8-year follow-up.

In conclusion, spinal meningeal melanocytoma inside the nerve root is rare and benign. It is difficult to diagnose and often misdiagnosed as schwannoma or meningioma due to its unspecific clinical manifestations and imaging characteristics. A precise diagnosis could be made based on histopathology. Positive response to HMB-45 favors the tumor of melanocytic origin, so it is suggested as a significant diagnostic marker for meningeal melanocytoma. Complete surgical resection is recommended as the primary treatment. Radiotherapy, chemotherapy and other treatments can be selected as adjuvant therapies, but their effects are controversial. The recurrence and metastasis rates also remain unclear. Accordingly, more treatment choices should be trialed and long-term follow-up undertaken. We believe that enriching clinical documentation and radiological data will polish our understanding on the pathophysiology and behavior of spinal meningeal melanocytoma.

Abbreviations

NSAIDs: non-steroidal anti-inflammatory drugs

CRP: C-reactive protein

ESR: erythrocyte sedimentation rate

EMA: epithelial membrane antigen

Declarations

Ethics and consent to partcipate

Not applicable

Consent to publish

The research was approved by ethics committee of Shanghai Longhua Hospital. Written informed consent was obtained from patients for publication of the cases report and any accompanying images.

Availability of data and materials

All supporting data can be provided upon request to the authors.

Competing interests

We declare that we have no competing interests.

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MCY and JHX designed the study. JMM a collected the data. MCY and JY wrote the manuscript. WM revised the manuscript. WM decided to submit the manuscript for publication.

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Table

Table 1 Summary of 13 cases of spinal meningeal melanocytoma

Authors	Year	Age	Gender	Location	Resection	Radiotherapy	Recurrence
Limas6	1972	71	M	C1	Autopsy	-	-
Ferracini7	1974	38	F	T11-L1	Subtotal	no	no
Graham8	1976	52	F	C7	Subtotal	no	no
Steinberg14	1978	71	F	T3	Subtotal	yes	yes
Verma9	1979	71	F	T2-3	Subtotal	yes	yes
Lach10	1988	20	F	C1-C2	Total	no	no
Cordoba13	1989	15	F	Cervical	Subtotal	no	yes
Kawara11	1989	38	F	C3-5	Biopsy	-	-
Tatagiba12	1992	40	M	C8	Total	no	no
Sankhla17	1994	19	M	C4-5	Subtotal	no	no
Ruelle15	1996	62	M	C1	Total	no	no
Czarnecki18	1997	69	F	T8-9	Total	no	-
Ibanez16	1997	44	F	T11	Total	no	no

Figures

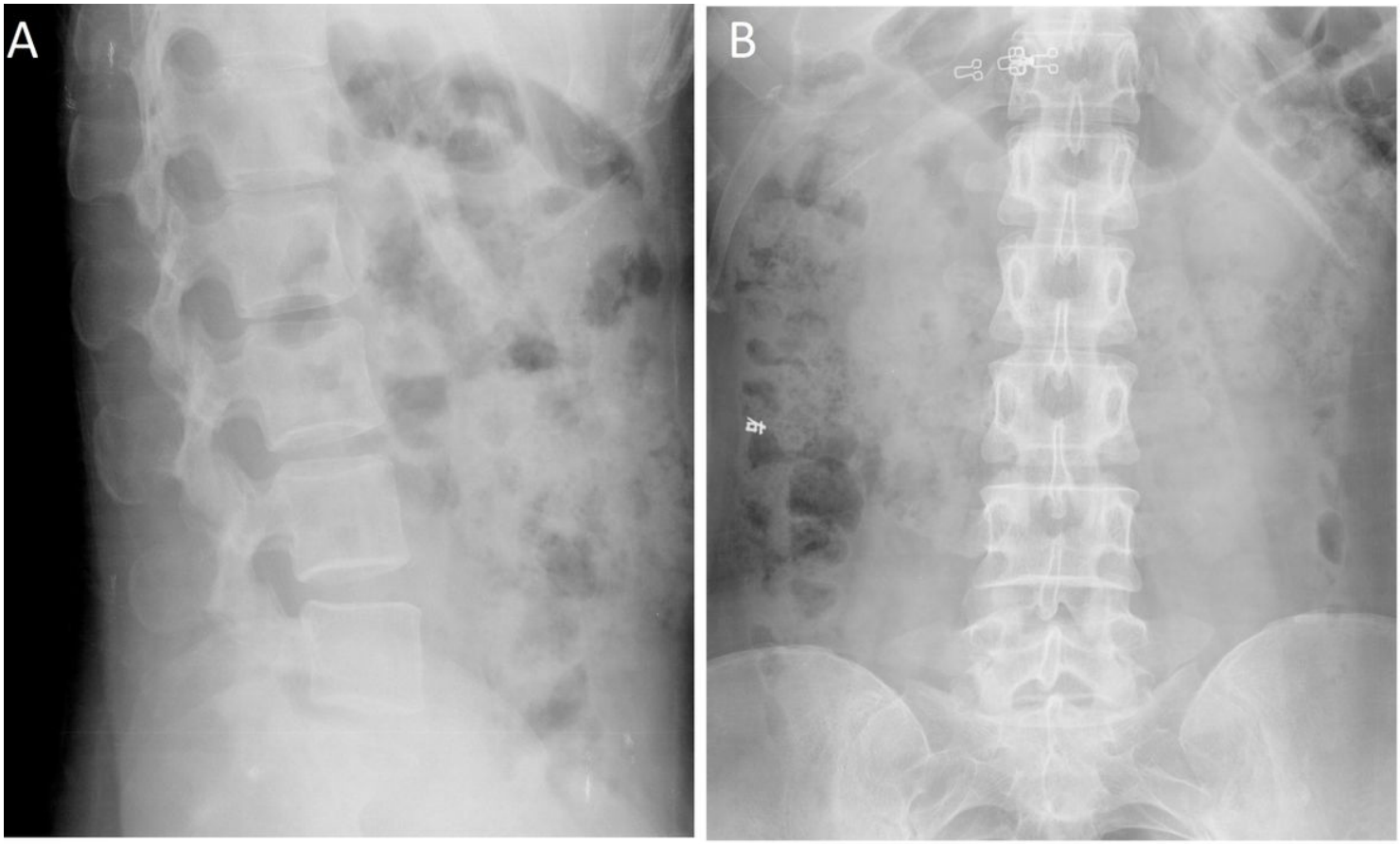

Figure 1

A-B The preoperative lumbar X-ray showed physiological radian is straight and tilt to the left side.

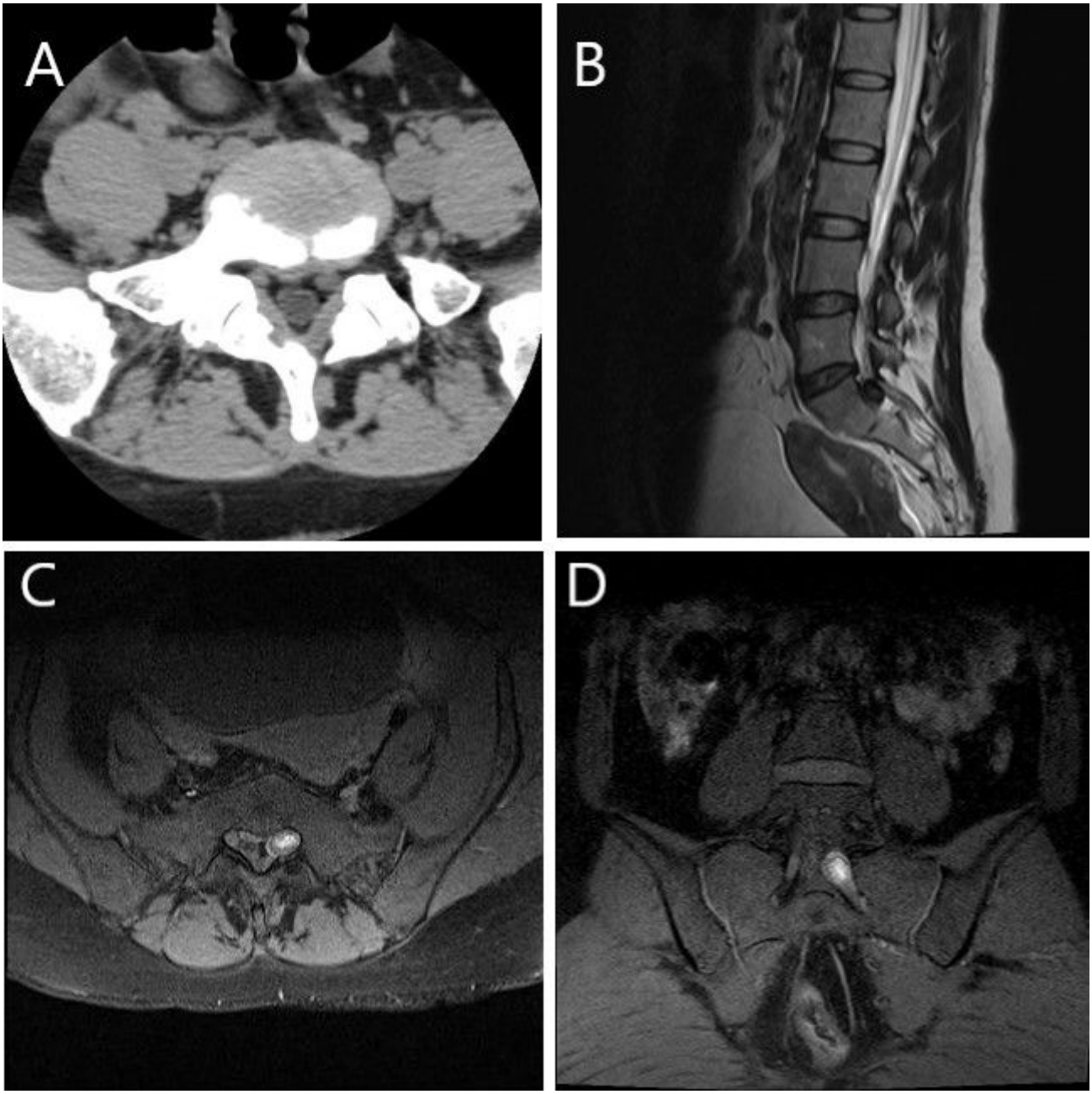

Figure 2

A-B On CT scan, the lesions at the S1 level are iso-density. Sagittal views of MRI the lesions at the S1 level displayed hypo-intense on T2-weighted imaging. C-D Axial and coronal views of MRI It demonstrated a hypo-intense lesion around the left S1 root and the lesions were obviously homogeneous enhanced.

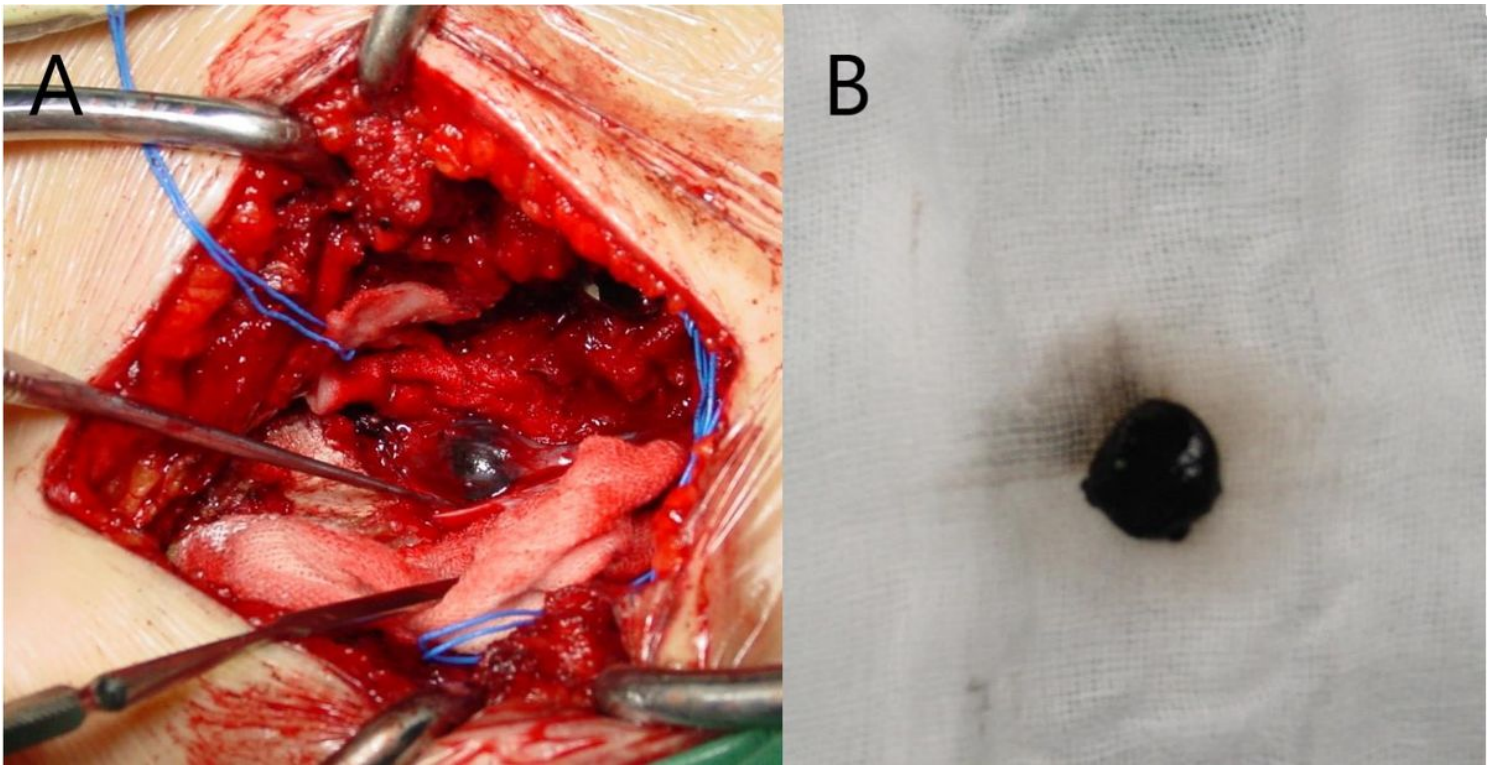

Figure 3

A-B At operation, a firm, dark brownish pigmented and large well-encapsulated lesions was adherent to the left S1 nerve root. And the tumor was En-bloc resected.

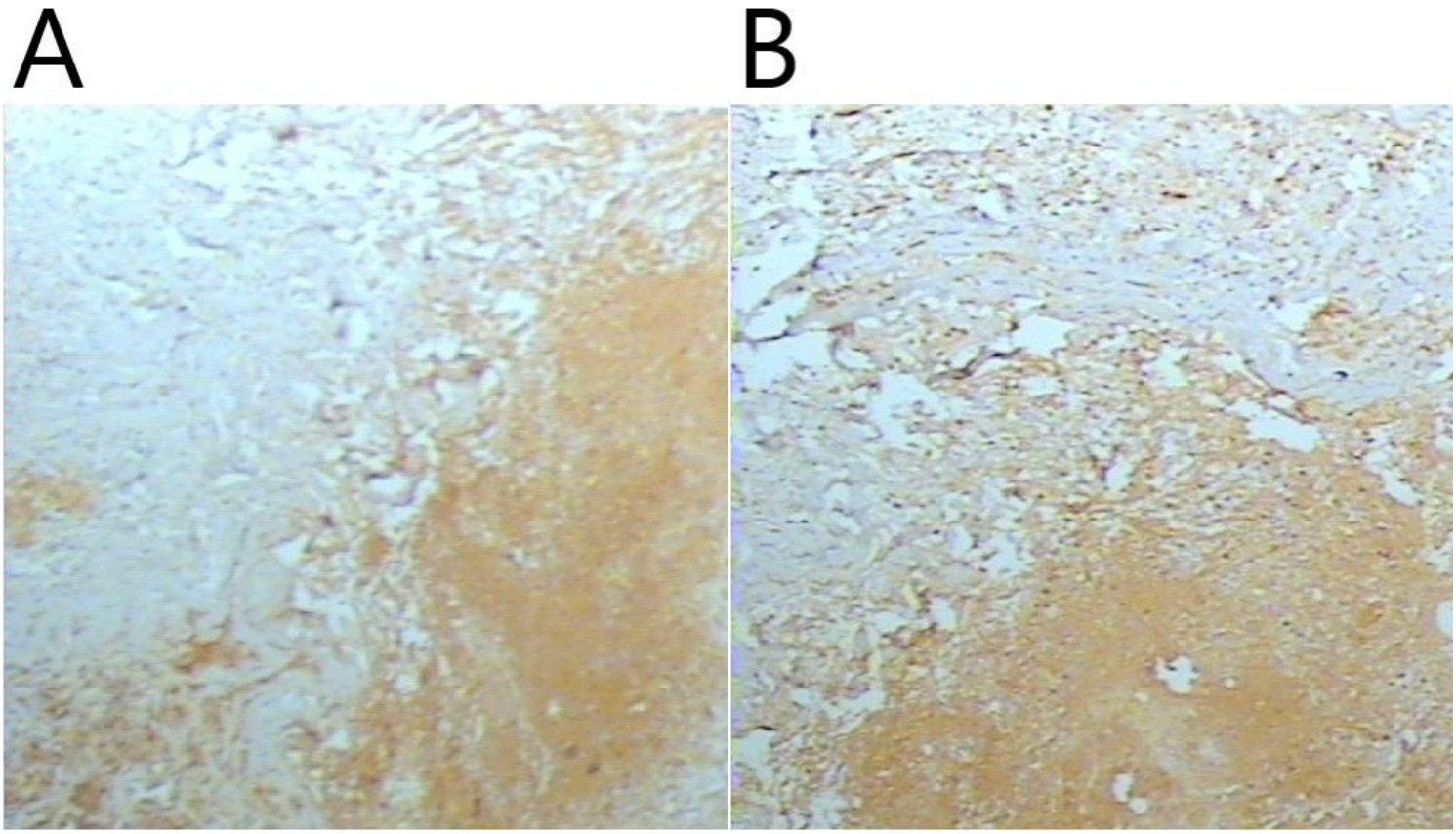

Figure 4

A-B Immunohistochemistry revealed that the tumor cells were positive for HMB-45 and S-100 protein.

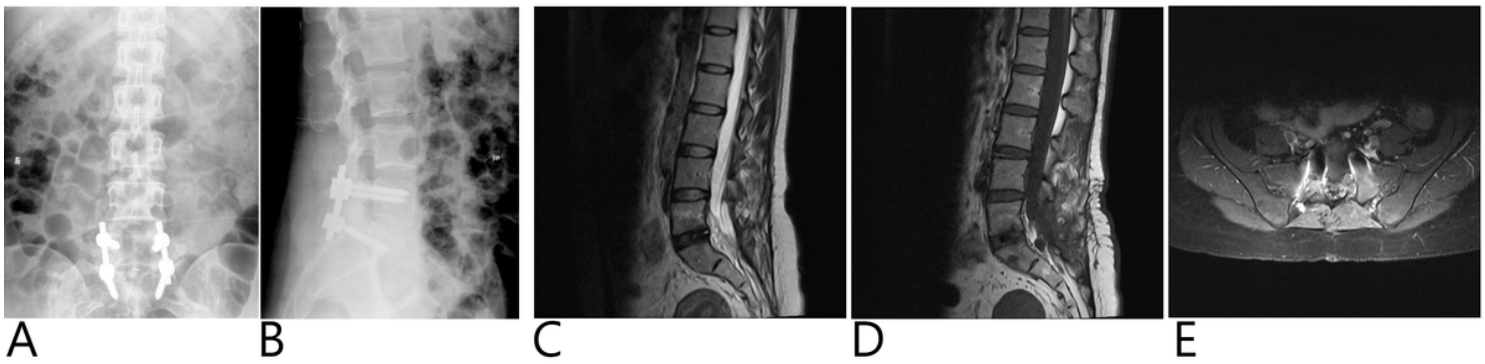

Figure 5

A-B Postoperative radiographs. PA and Lateral views 8 years after surgery showed no spinal instability. C-E Sagittal and axial views of MRI, no signs of local recurrence were observed.

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